PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

# PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

| | |
|---|---|
| Applicant's or agent's file reference<br>GP05-1009PCT | Date of mailing *(day/month/year)*<br>FOR FURTHER ACTION<br>See paragraph 2 below |

| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/JP2005/003651 | 03.03.2005 | 03.03.2004 |

International Patent Classification (IPC) or both national classification and IPC

Applicant

MITSUBISHI KAGAKU BIO-CLINICAL LABORATORIES, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| Name and mailing address of the ISA/JP | Authorized officer |
|---|---|
| Facsimile No. | Telephone No. |

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/JP2005/003651

**Box No. I Basis of this opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/003651

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 4-12, 15 | YES |
| | Claims | 1-3, 13, 14 | NO |
| Inventive step (IS) | Claims | 4, 5, 7-12 | YES |
| | Claims | 1-3, 6, 13-15 | NO |
| Industrial applicability (IA) | Claims | 1-15 | YES |
| | Claims | | NO |

2. Citations and explanations:

Document 1: "Saliva concentration of some Selected Proteins and Glycoprotein Markers in Man after Supplementary Intake of β-Carotene," (IUMIKARI et al), International Journal of Vitamin and Nutrition Research, 1988, Vol. 58, No. 2, pages 171-177

Document 1 (see, summary, and page 173, lines 7-22) describes that (1) a rise in β-Carotene concentration in saliva can be detected in correlation with a rise in β-Carotene concentration in serum by intake of β-Carotene, and that (2) a measurement of changes in β-Carotene concentration is performed with reference to a mean value of the placebo treated group. Furthermore, document 1 describes that after gathered saliva is extracted with n-hexane, the measurement of β-Carotene is performed by analyzing the extract by HPLC.

The subject matters of claims 1-3, 13 and 14 do not appear to be novel in view of document 1.

The subject matter of claim 6 does not appear to involve an inventive step in view of document 1.

Since document 1 describes that β-Carotene concentration in saliva is raised in response to intake of β-Carotene, a person skilled in the art could have easily determined whether the intake or intake amount of β-Carotene based on the β-Carotene concentration in saliva is adequate or not.

The subject matter of claim 15 does not appear to involve in inventive step in view of document 1.

Since document 1 describes that β-Carotene concentration in saliva is raised in correlation with β-Carotene concentration in blood plasma, a person skilled in the art could have easily evaluated the effect of a medicine or health supplement when ingested, and performed screening for the medicine or health supplement by using the β-Carotene concentration in saliva as an indicator.

None of the documents cited in the ISR describes examining the effect or the action on the in- vivo synthesis or metabolism of any fat- soluble vitamin and/or fat- soluble food factor in an administered therapeutic agent, such as a fat- soluble vitamin and/or fat- soluble food factor in saliva is analyzed as an indicator in the subject matters of claims 4, 5 and 7. Furthermore, it is not considered to be obvious to a person skilled in the art.

None of the documents cited in the ISR describes examining any fat- soluble vitamin and/or fat- soluble food factor in vivo, such as a fat- soluble vitamin and/or fat- soluble food factor in

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

parotid saliva is analyzed in the subject matters of claims 8-12. Furthermore, it is not considered to be obvious to a person skilled in the art.